PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 1094WOORD01	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP03/01876	International filing date *(day/month/year)* 25.02.2003	Priority date *(day/month/year)* 06.03.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/4425		
Applicant ALTANA PHARMA AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the International application

Date of submission of the demand	Date of completion of this report
20.09.2003	03.12.2003
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Sindel, U Telephone No. +49 89 2399-7064

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP03/01876

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-57 as originally filed

Claims, Numbers

1-47 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 35-38

   because:

   ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	7-14, 19-27, 30-34 (YES)
	No:	Claims	1-6, 15-18, 28, 29,35 (NO)
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-47 (NO)
Industrial applicability (IA)	Yes:	Claims	1-34, 39-47 (YES)
	No:	Claims	

2. Citations and explanations

   see separate sheet

Item III

Claims 35-38 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Item V

1. Reference is made to the documents cited in the search report. They are numbered accordingly.

2. **Novelty**

The subject matter of claims 1-6, 15-18, 28, 29 and 35 is not regarded as new in the sense of Article 33(2) PCT.

D1 already discloses a pharmaceutical composition comprising a PDE4 inhibitor (nimesulide) and a histamine (H1) receptor antagonist (cetirizine dihydrochloride) in a tablet (see page 3, lines 57-58; page 4, lines 16-18 and lines 26-29 as well as example I) which is used for the treatment of allergic disorders like rhinitis, bronchitis and asthma (see page 2, lines 10-11). As first production step of this tablet, the mixing of the active ingredients is mentioned (see example I). Hence, the subject matter of claims 1-6, 15- 18 and 35 is not new.

D2 also describes a combination of a histamine (H1) receptor antagonist (here: terfenadine) with nimesulide (PDE4-inhibitor - see D1) for the treatment of allergic rhinitis (see summary). Nimesulide and terfenadine were applied separately by giving two tablets to the group of patients (see page 314, 1st column, last paragraph). Hence, the subject matter of claims 1-3, 17-18, 28-29 and 35 is not new.

3. **Inventive step**

The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of claims 1-47 does not involve an inventive step in the sense of Article 56 EPC.

Closest prior art is D1 which discloses a composition comprising a PDE4-inhibitor and a histamine H1 receptor antagonist for the treatment of allergic disorders like rhinitis, bronchitis and asthma (see page 2, lines 5-11).

The problem underlying the present application in view of the prior art is therefore the provision of a superior composition for the same purpose.

The solution presented by the applicant can not be regarded as being inventive since it is just a combination of well-known active compounds from the classes of PDE4- or PDE3/4- inhibitors and histamine H1 receptor antagonists.

D4: loratadine is a H-1 histamine receptor antagonist which is effective in treating allergic rhinitis and asthma (see column 1, lines 16-22 and lines 54-63).

D5: roflumilast is a selective PDE4-inhibitor which can be used in the manufacture of a medicament for the treatment of chronic inflammatory disorders such as asthma and chronic obstructive pulmonary disease (see abstract).

D6: tetrahydro-2H-phtalazine-1-one derivatives are effective PDE4-inhibitors for the treatment of disorders of the respiratory tract (see examples 1-10, page 17, paragraph 6 and page 18, first paragraph).

Consequently, in the absence of any surprising effect, the subject matter of claims 1-47 does not involve an inventive step.

4. Industrial applicability

For the assessment of the present claims 35-38 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.